REMARKS

The claims remaining pending in this application, claims 217-219, 225, 238 and 277, have been finally rejected under 35 USC § 112, first and second paragraphs. These rejections are respectfully traversed, and reconsideration is requested in light of the amendments made herein and the arguments presented below.

Applicants' amendment of certain rejected claims is not to be construed as an admission that the Examiner's rejections were proper. The Applicants continue to believe that the rejected claims are described in and enabled by the specification, as previously argued. The rejected claims have been amended for the sole purpose of advancing the case to allowance. The Applicants reserve the right to file one or more continuing applications to continue the prosecution of the rejected claims.

Substance of the Telephonic Interview

The Applicants express appreciation for the telephone interview their undersigned attorney conducted with the Examiner on July 30, 2010. The Applicants' attorney discussed the preferred embodiments of the invention with the Examiner. The conversation also included a discussion of how to claim the instant invention using the specific sequences disclosed in the specification with enough scope to protect the invention. The Examiner noted potential difficulties in the avoidance of a new matter rejection.

Further discussion of the telephone interview can be found in the accompanying Declaration Under 37 CFR § 1.132 by co-inventor Dr. Michael Valentine Agrez, which will be referenced below.

Claim Amendments

Claim 217 has been amended to recite that the linear polypeptide of the "providing" step now comprises an amino acid sequence selected from a defined Markush group of six elements. The first three elements of the Markush group are the sequences defined by SEQ ID No. 2 (RSKAKWQTGTNPLYR), SEQ ID No. 22 (RARAKWDTANNPLYK) and SEQ ID No. 23 (RSRARYEMASNPLYR). The other three elements of the Markush group are the sequences defined by SEQ ID No. 2 (RSKAKWQTGTNPLYR), SEQ ID No. 22 (RARAKWDTANNPLYK)

and SEQ ID No. 23 (RSRARYEMASNPLYR) ***wherein "the linker sequence of the binding domain is deleted*** such that the ***opposite terminal end*** amino acid sequence regions of the binding domain ***remain and are contiguous with one another*** in the polypeptide." Markush group element no. 4, then, is exemplified by SEQ ID No. 3 (RSKAKNPLYR), and Markush group elements 5 and 6 are exemplified by analogy with SEQ ID No. 3, as supported in the specification and explained further in the accompanying Agrez Declaration, as will be described below.

Claim 219 has been amended to depend also from claim 217, which dependency was omitted from the previous amendment.

Claim 277 has been amended to recite that the polypeptide of any one of claims 217, 218 or 219 is "between 10 and 25 amino acids in length." Support for claim 277 is provided, e.g., at page 49, lines 21-23, of the specification, where it is stated that, preferebly, the length of a polypeptide of the invention will be from about "5 amino acids" to about "25 amino acids" in combination with p. 50, lines 1-2, where it is stated that, preferebly, the polypeptide "will comprise [...] the amino acid sequence RSKAKNPLYR" (SEQ ID No. 3), which, at 10 amino acids, represents a specifically disclosed lower limit ***within*** the polypeptide length range of 5 amino acids to 25 amino acids.

Thus, Applicants submit that no new matter has been introduced by these claim amendments.

Rejections under 35 U.S.C §112, First and Second Paragraph

Claims 217-219, 225, 238 and 277 continue to be rejected for lack of written description support and for lack of enablement. As independent claim 217 has been amended substantially from its form when rejected, substantial reference will be made to the Agrez Declaration to show that the amended claims are fully described in and supported by the specification as filed, that the full breadth of the amended claims is enabled by the specification, and that the Examiner's questions have been answered.

The Agrez Declaration, with annotations in **BOLD**, states:

3. I am a co-inventor of the subject matter described and claimed in the above-identified patent application.

4. I have read and understood the Office Actions of the Examiner, including the Office Action mailed June 9, 2010.

5. In the Office Action of June 9, 2010, the Examiner acknowledged the instant specification teaches that SEQ ID No. 2 (RSKAKWQTGTNPLYR), SEQ ID No. 22 (RARAKWDTANNPLYK) and SEQ ID No. 23 (RSRARYEMASNPLYR) bind to the MAP kinase Erk2. As explained in the instant application, e.g., at pp. 86 and 92, SEQ ID No. 2 was isolated from the cytoplasmic tail of the β6 integrin subunit and provides a binding domain of the β6 integrin subunit for Erk2. Likewise, SEQ ID No. 22 was isolated from the cytoplasmic tail of the β3 integrin subunit and provides a binding domain of the β3 integrin subunit for Erk2, and SEQ ID No. 23 was isolated from the cytoplasmic tail of the β5 integrin subunit and provides a binding domain of the β5 integrin subunit for Erk2. **[SEQ ID Nos. 2, 22 and 23 are elements 1-3 in the Markush group now recited in claim 217.]**

6. The Examiner also acknowledged her understanding that SEQ ID No. 3 (RSKAKNPLYR) is derived from the β6 integrin subunit and represents SEQ ID No. 2 with a deletion of the linker amino acids WQTGT. The Examiner commented, however, that although the specification stated that evidence of binding of Erk2 to the β3 and β5 integrin binding domain peptides was found, the specification failed to state if the corresponding amino and carboxy terminal regions in those β3 and β5 peptides would bind to Erk2 *out of context* of their positions in their respective binding domain when the intervening linker amino acids in those binding domains were deleted. **[SEQ ID No. 3 (RSKAKNPLYR) exemplifies element 4 in the Markush group now recited in claim 217.]**

7. In a telephone conversation with the Applicants' attorney on July 30, 2010, the Examiner suggested that declaration evidence, showing that the β3 and β5 peptides without the linker sequences perform as the Applicants had asserted, would advance the prosecution of the instant application. **[The β3 and β5 peptides (SEQ ID No. 22 and SEQ ID No. 23)**

without the linker sequences exemplify elements 5 and 6 in the Markush group now recited in claim 217.]

8. I report herein that experiments I have conducted or which have been conducted under my direction, show that the β3 derived peptide RARAKNPLYK represented by the SEQ ID No. 22 peptide with a deletion of the linker amino acids WDTAN, and the β5 derived peptide RSRARNPLYR represented by the SEQ ID No. 23 peptide with a deletion of the linker amino acids YEMAS, both inhibit the growth of cancer cells.

9. In particular, Graph A in Annexure MVA-1 attached to this declaration shows that the polypeptide AAVALLPAVLLALLARARAKNPLYK (IK3), comprising the β3 derived peptide RARAKNPLYK coupled to the partial signal peptide AAVALLPAVLLALLA and administered via subcutaneous injection to Balb/c nude mice daily over a period of 5 days at a dosage of 12 mg/kg body weight in physiological saline, inhibited the growth of DU145 human prostate cancer cell xenographs compared to normal saline alone. The partial signal peptide AAVALLPAVLLALLA was used as a "facilitator moiety" to facilitate passage of the RARAKNPLYK peptide across the outer cell membrane into the cytoplasm of the cancer cells.

10. Further, Graph B in Annexure MVA-1 shows that SEQ ID No. 23 (RSRARYEMASNPLYR) and the β5 derived peptide RSRARNPLYR coupled to the partial signal peptide AAVALLPAVLLALLA (respectively designated nf-b5-frag5 and nf-b5-10-4 in Graph B), each inhibit the proliferation of HT29 human colon carcinoma cells in an MTT cell proliferation assay. To prepare the MTT solution for use in the assay, 100 mg of MTT (methylthiazoletetrazolium) was mixed with 20 ml of phosphate buffered saline (PBS) at pH 7.4. The resulting solution was filter sterilized (0.2 μM syringe filter), stored at 4°C and protected from light until use. MTT substrate is cleaved in growing cells to yield a water insoluble salt. After solubilisation of the salt, a coloured product is produced that allows quantitation of the proliferative activity of the cells. As also shown in Graph B,

while both of the administered peptide agents inhibited proliferation of the cancer cells, a greater degree of inhibition was observed for the peptide agent comprising RSRARNPLYR.

11. These results show that like SEQ ID No. 3 (RSKAKNPLYR), each of the RARAKNPLYK and RSRARNPLYR peptides inhibit the growth of cancer cells.

12. Simple sequence alignment shows 80% amino acid sequence identity between SEQ ID No. 3 (RSKAKNPLYR) and the RARAKNPLYK peptide, and also between peptides RARAKNPLYK and RSRARNPLYR. Further, a sequence identity of 70% exists between SEQ ID No. 3 (RSKAKNPLYR) and peptide RSRARNPLYR. In addition, the Examiner will note the sequence identity between the 5 C-terminal amino acids of these three peptides is 80% to 100%.

13. The high level sequence identity that exists between SEQ ID No. 3 (RSKAKNPLYR) and the RARAKNPLYK and RSRARNPLYR peptides does not exist between the deleted linker sequences WQTGT, WDTAN and YEMAS.

14. Thus, it is clear that the linker amino acids of SEQ ID No. 2 (RSKAKWQTGTNPLYR), SEQ ID No. 22 (RARAKWDTANNPLYK) and SEQ ID No. 23 (RSRARYEMASNPLYR) are not conserved, and like amino acids WQTGT in SEQ ID No. 2, the WDTAN and YEMAS linker amino acids in SEQ ID No. 22 and SEQ ID No. 23 peptides are also not important to, or required for, inhibition of cancer cell growth.

15. That SEQ ID No. 3 (RSKAKNPLYR) and the RARAKNPLYK and RSRARNPLYR peptides retain cancer cell growth inhibitory activity may be explained by the β6, β3 and β5 binding domains for Erk2 each forming a respective "loop" comprising the linker amino acids of the binding domain, thereby drawing the opposite end regions of the binding domain linearly together.

Summary

Thus, Applicants submit that the method of the instant invention is claimed with particularity, using the specific sequences disclosed in the specification. Elements 1-3 of the recited Markush group in amended claim 217 are defined, in order, by SEQ ID Nos. 2, 22 and 23. Elements 4-6 of the recited Markush group in amended claim 217 are exemplified, in order, by SEQ ID No. 3, the sequence RARAKNPLYK and the sequence RSRARNPLYR. Dr. Agrez showed by the experiments that he conducted that RARAKNPLYK, which is the β3 derived peptide represented by the SEQ ID No. 22 peptide with a deletion of the linker amino acids WDTAN, and RSRARNPLYR, which is the β5 derived peptide represented by the SEQ ID No. 23 peptide with a deletion of the linker amino acids YEMAS, ***both inhibit the growth of cancer cells***, as had been reported in the specification for SEQ ID No. 3 (or RSKAKNPLYR), the β6 derived peptide represented by the SEQ ID No. 2 peptide with a deletion of the linker amino acids WQTGT.

Thus, Applicants submit that the amended claims are fully described in and enabled by the specification, and that all claims are in condition for allowance. Such action is respectfully requested.

The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

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